Claim 46, line 2, change "rat-6" to "rat".

IN THE DRAWINGS

Change Fig. 1 to Fig. 1 A.

R E M A R K S

In his action of September 19, 1994, the Examiner notes that the amendment proposed in pages 17 to page 18 was incorrect. Applicant has made the suggested change in location so that the amendment is clear.

Applicant has proposed to change the Drawing of "Fig. 1" to "Fig. 1A" so that it accords with the identification of the text of the specification (See page 5, line 32). It is requested that this change not be made until such time there is allowable subject matter.

The Examiner has continued his rejection of claims 37-39 as lacking support. This rejection is respectfully traversed. Applicant's reference to subpart (a) of issued claim 1 of U.S. Patent 4,980,281 (the parent case) was to demonstrate that the language of subpart (a), per se, was no different from what had already been accepted. Insofar as the support for the use of the method invention without necessarily using a control, or second, cell, applicant responds further.

It is apparent that the use of a control cell is only to provide confidence that the observed change in phenotypic characteristic of the Test cell is actually in response to the overproduced protein of the Test cell. That is, the basic concept of the invention is clearly stated without reference to a control cell as such:

> In brief, the method which we describe herein involves the generation of a [Test] cell line purposefully engineered to detect both stimulatory and inhibitory agents which are absolutely specific for any given protein which

affects the cultural or morphological characteristics of the cell.

The basis for this invention is my observation that if a protein (the "protein of interest", or POI) which is involved in some manner in cellular growth control is overproduced in cells, then pharmacologic agents which can activate or inhibit the POI can result in altered growth properties of the cells.

Page 3, line 34 to page 4, line 11.

A control cell would be a suitable way of affirming that the Test cell is "involved in some manner in cellular growth control." However, in instances where the ability of the overproduced protein to effect a phenotypic characteristic of a Test cell is already established (as from prior testing or from the literature), it is obviously not necessary to physically establish that fact yet again by continuing to use a control cell line each time a new substance is investigated. It is helpful, but not necessary. As explicitly demonstrated by applicant (see below), one can screen for suspected inhibitors or activators with the Test cell alone.

For example, in the Test cell work of Table 3 of the application, in which the method of the invention is used to determine the ability of various substances, such as tamoxifen, to inhibit a responsive phenotypic characteristic (growth in agar), of a Test cell, without the specific use of a control cell. It is also reflected in the teachings of the specification at page 21, lines 1-14, wherein it is plainly shown that once one has identified a cell line with the required growth characteristics, the testing is simply between the unknown or suspected inhibitor/activator and the Test cell. This confidence in the test cell characteristics is an inherent feature of all claims since the process of "providing a first cell which overproduces said protein and exhibits said

phenotypic characteristic in response to the protein" necessarily includes a selection process in which it is the protein and not other spurious agents or reactions which are responsible for the observed effects.

Applicant submits that the claims now at issue define the invention in a manner fully supported by and consistent with the specification. In this regard, the applicant respectfully notes that the Examiner's reference to Table 3 as showing that "known inhibitors of PKC affect the growth of the [Test] cell lines as expected" refers only to H7, not tamoxifen. Indeed, except as provided by the results of the testing reported by the applicant in the description of his invention, tamoxifen, for example, was not known to be an inhibitor of PKC in cell culture. It is in fact a very specific example of how the invention can be used to determine whether a particular substance is an inhibitor or activator as required by the preamble of the claims, and is indeed, an example of the success of the process in discovering such useful properties in a substance which was not otherwise known to possess them. The Examiner is respectfully referred to page 39, lines 3-6, which are reproduced here for convenience: "Inhibition of the growth of the R6-PKC3 cells in agar in the presence of tamoxifen provided critical evidence that tamoxifen could inhibit PKC-mediated stimulation of cellular growth." However, it must also be understood that not every case of the invention results in such a success. That is, in practice, a particular test substance may be found to have no inhibition or activation property, but this is in itself a useful, though negative, result which can be readily observed according to the invention in an efficient and expeditious way.

The Examiner has rejected claim 48 as lacking support in that there is no assurances of public availability of the recited cell strains. Strains of normal rat kidney fibroblasts

(Cat # CRL-1570) and Chinese Hamster Ovary (CHO-K1) cells (Cat. # CCL-61) are available from the ATCC. FDC-P1 cells are available from Dr. Andrew Kraft at the University of Alabama at Birmingham.

The Examiner has rejected several claims on failure to comply with the second paragraph of §112.

With regard to claim 32, applicant has amended the claim to insert the language necessary to provide the requested congruency.

With regard to the breadth of claim 37, applicant respectfully requests reconsideration. It is emphasized that there is no requirement of the invention that the presence of the protein be due to a "genetically altered" cell. Plainly this is one method of obtaining the protein. The Examiner has not shown how the prior art would preclude coverage of proteins provided by alternate techniques. The pioneering nature of the invention should not be limited to a specific manner of providing the protein as this would unduly limit the scope of the invention. The Examiner's attention is called to the fact that the claims of the parent patent (U.S. Patent 4,980,281) do not require the limitation now being suggested, and it plainly was not required that applicant be compelled to limit his broad claims to the preferred method of providing the protein. The essence of the invention does not lie in the particular manner by which the protein is provided, but rather in the use of the protein--no matter how provided--as a tool which evokes in and of itself a phenotypic change in the cell which can be stimulated or inhibited by treatment of various substances.

With respect to the prior art, the applicant acknowledges the withdrawal of rejections based on Sonnenschein, et al., Chou, and Penman et al. The Examiner has repeated his rejection of claims as anticipated by (§102(e)), or obvious in

light of (§103), Knight et al. Applicant respectfully traverses this rejection.

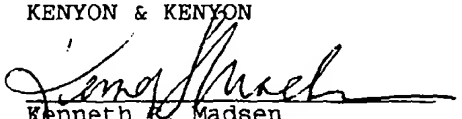
The Examiner has stated that he disagrees that Knight et al. do not teach a "responsive change in a phenotypic characteristic other than the level of said protein in said cell per se" because "the expression of another indicator protein, [e.g., p24] which is not the target protein, can be assessed." This, however, is not a phenotypic characteristic which is responsive to inhibitors or activators of the TAT protein which arises solely because of the expression of TAT. Indeed, these investigators specifically use the well known transactivating property of the TAT protein on the HIV LTR in order to develop a standard reporter gene assay, the latter being a well known approach. The power of the present invention, however, unlike Knight et al., is that no such reporter gene construct is necessary, nor is knowledge of the biological function(s) of the target protein required.

The Examiner has stated that "applicant's own system does not directly analyze the target protein of interest but rather, a phenotypic characteristic." Applicant respectfully disagrees, however, because applicant first defines a phenotypic characteristic which results solely from the overproduction of the target protein and then establishes that said phenotypic characteristic is responsive to suspected inhibitors or activators as desired of said overproduced target protein. This is what applicant means by a "responsive" change in a phenotypic characteristic. Such a concept is not found in the teachings of Knight et al.

For the reasons provided above, the applicant submits he has met all the objections of the Examiner and that the claims as amended are in a condition for allowance.

Respectfully submitted,

KENYON & KENYON



Kenneth R. Madsen
Registration No. 20,721

One Broadway
New York, NY 10004
212-425-7200

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